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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/313,942	05/19/99	STAHL	N REG-203-A

HM22/1002

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EXAMINER	
O HARA, E	
ART UNIT	**PAPER NUMBER**
1646	18

DATE MAILED: 10/02/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/313,942	Applicant(s) STAHL ET AL.	
	Examiner Eileen B. O'Hara	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *9 July 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *16* .
4) ☒ Interview Summary (PTO-413) Paper No(s). *13* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Prosecution Application

1. The request filed on July 9, 2001 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/313,942 is acceptable and a CPA has been established. An action on the CPA follows.

Terminal Disclaimer

2. The terminal disclaimer filed on July 9, 2001 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of any patent granted on Application Number 08/563,105, Patent Number 5,844,099 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Advisory Information

3. In the preliminary amendment submitted July 9, 2001, Applicants requested the addition to the first line of the specification to add continuation data claiming priority to USSN 09/313,942. However, the application retains the original application number, so the amendment was not necessary and was not entered.

Withdrawn Rejections

4. The rejection of claims for double patenting is withdrawn in view of Applicants' terminal disclaimer.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid molecule encoding a fusion polypeptide capable of binding a cytokine to form a nonfunctional complex comprising a first fusion polypeptide component comprising the amino acid sequence of the cytokine binding portion of the extracellular domain of the specificity determining component of the cytokine's receptor, a second fusion polypeptide component comprising the amino acid sequence of the cytokine binding portion of the extracellular domain of the signal transducing component of the cytokine's receptor, and a third fusion polypeptide component comprising the amino acid sequence of a multimerizing component, with the limitation that the fusion polypeptide is derived from a cytokine receptor that has those two extracellular components, does not reasonably provide enablement for fusion proteins comprising the two extracellular components, as described above, of a cytokine receptor that does not have separate specificity determining components and signal transducing components. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The specification teaches that the family of cytokines, called the CNTF family, are

grouped together because of their distinct structural similarities and because they activate receptors by binding to β components that result in homo or heterodimerization of these β components. The specification further teaches that in addition to these β components, some of these cytokines also require specificity-determining "α" components that are more limited in their tissue distribution than the β components, and thus determine the cellular targets of the particular cytokines. For example, CNTF requires CNTFRα, and IL-6 requires IL-6α, and both CNTFRα and IL-6α can function as soluble proteins, consistent with the notion that they do not interact with intracellular signaling molecules but that they serve to help their ligands interact with the appropriate signal transducing β subunits. On page 3 the specification teaches that in addition to homo- or hetero-dimerization of β subunits as the critical step for receptor activation, a second important feature is that formation of the final receptor complex by the CNTF family of cytokines occurs through a mechanism whereby the ligand successively binds to receptor components in an ordered manner, in which CNTF first binds to CNTFRα, forming a complex which then binds pg130 to form an intermediate (called the αβ1 intermediate) that is not signaling competent because it has only a single β component, before finally recruiting LIFRβ to form a heterodimer of β components which then initiates signal transduction. The specification discloses that these findings led to a proposal for the structure of a generic cytokine receptor complex, shown in Figure 1, in which each cytokine can have up to 3 receptor binding sites: a site that binds to an optional α specificity-determining component (α site), a site that binds to the first β signal-transducing component (β1 site), and a site that binds to the second β signal-transducing component (β2 site). These three sites are used in sequential fashion, with the last step in complex formation – resulting in β component dimerization – critical for initiating signal

transduction. This is enabled for a fusion polypeptide derived from a receptor such as the IL6 receptor, which has α and β components that comprise the functional domains recited in claim 1. However, the dependent claims are directed to a large number of other cytokine receptors, some of which do not have the required structural features to enable construction of the fusion polypeptide as claimed. For example, in the Leukocyte Antigen FactsBook, Barclay et al., editors. Academic Press, Harcourt Brace Jovanovich, Publishers, 1993, the structures of various other cytokine receptors that are claimed are shown on pages 162, 166, 188, 290, 320, 322, 330, 338 and 410. These cytokine receptors are CD28(binds B7), CD30(NGFR superfamily), CD40(NGFR superfamily), CTLA-4(binds B7), IFNγR, IL1R, IL4R, IL7R, TNFR1 and TNFRII, for example, are either single chain receptors or homodimers, and do not possess the requisite first component comprising the sequence of the cyokine binding portion of the extracellular domain of the specificity determining component, and the second component of the cytokine binding portion of the extracellular domain of the signal transducing component of the receptor. The specification does not teach how to make the claimed construct for such receptors.

Recitation in claim 1 of an appropriate structural limitation regarding the structure of the receptor would obviate the rejection, and the deletion of cytokine receptors in the dependent claims that do not possess the necessary structural features would be required to allow those claims.

Conclusion

6. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (703) 308-3312. The examiner can normally be reached on Monday through Friday from 9:00 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564.

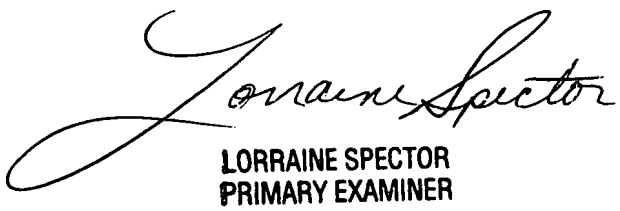
Official papers filed by fax should be directed to (703) 308-4242.

Informal papers filed by fax should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Eileen B. O'Hara, Ph.D.

Patent Examiner



LORRAINE SPECTOR
PRIMARY EXAMINER